Appl. no. 09/738,540 Amdr. dated 7/11/2003 Reply to Office action of 2/11/03

## Amendments to the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

# Listing of Claims:

- 1. (Currently amended) A method of treating rheumatoid arthritis, comprising administering to a mammal in need thereof effective amounts of an anti-CD11a antibody and a TNF-α antagonist wherein the TNF-α antagonist is a TNF-α receptor 1 G Fc fusion protein.
- 2-5. (Canceled)
- 6. (Previously presented) The method of claim 1, wherein the anti-CD11a antibody is a non T-cell depleting antibody.
- 7. (Presently canceled) The method of claim 1, wherein the TNF- $\alpha$  antagonist is an immunoadhesin.
- 8. (Presently canceled) The method of claim 7, wherein the immunoadhesin is a fusion of at least a TNF-α binding portion of a TNF-α receptor and an immunoglobulin constant domain sequence.
- (Presently canceled) The method of claim 8, wherein the immunoadhesin is a TNFα receptor - IgG Fc fusion protein.
- 10-17. (Cancelled)
- 18. (Currently amended) The method of claim [[9]] 1, wherein the fusion protein consists of the extracellular ligand binding portion of human tumor necrosis factor receptor linked to the hinge region, CH2 and CH3 domains of human IgG1.
- 19. (Currently amended) The method of claim 1 or claim 18, further comprising administering to the mammal an effective amount of methotrexate.
- 20. (Previously presented) The method of claim 1 or claim 9, wherein the anti-CD11a antibody is a humanized antibody.
- 21. (Withdrawn) The method of claim 1, wherein the TNF- $\alpha$  antagonist is an anti-TNF- $\alpha$  antibody.

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#### **REMARKS / ARGUMENTS**

## Status of the claims

Claims 1, 6-9 and 18-25 have been examined and are rejected on various grounds. These rejections are addressed in the appropriate sections below. Claims 21-23 have been withdrawn from further consideration as being drawn to a nonelected invention.

By virtue of this amendment, claims 1, 18 and 20 are amended, and claims 7, 8, and 9 are canceled. Upon entry of this amendment, claims 1, 6, 18-20 and 24 will be pending. Claim 1 has been amended to incorporate the description of claim 9. Claims 18 and 20 have been amended to recite the proper claim dependency upon the cancellation of base claim 9. The amendments to the claims have been made in an effort to place them in condition for allowance or in better form for appeal. The claim amendments are not to be construed as an agreement or acquiescence of the correctness of the rejection or of the Examiner's position. Applicants reserve the right to prosecute the cancelled subject matter at a later date. No new matter has been introduced by the above amendments.

Entry of these amendments and reexamination and reconsideration of the claims, as amended, are respectfully requested.

### Rejections under 35 U.S.C §112, first paragraph

Claims 1, 6-8 and 19 have been rejected under 35 U.S.C §112, fit st paragraph on various grounds. The Examiner acknowledges that Applicants are in possession of a method of treating rheumatoid arthritis comprising administering to a mammal in need there of effective amounts of an anti-CD11a antibody and a TNF-α receptor - lgG Fc fusion protein. However, the Examiner comments that the claims encompass a broad genus of TNF-α antagonists with unlimited number of possibilities with regard to the length of the TNF-α binding portion of the TNF receptor. In addition, it is remarked that the specification does not provide sufficient guidance as to which amino acids of TNF-α would have been altered such that the resultant molecule would retain the function to transduce cytotoxic and proliferative signals.

Applicants remark that for the purposes of the present methods of the invention, the TNF- $\alpha$  antagonists function to compete for binding to TNF- $\alpha$ , thus blocking the binding of the ligand to its native receptor on cells. The TNF- $\alpha$  antagonist serves as a blocker; it is not being relied upon to transduce cytotoxic and proliferative signals. Thus, it is not necessary for the specification to teach the parts of the receptor that would retain these functions. TNF receptors